REMARKS

Claims 1-4, 38-41, 57-59 and 68 have been allowed. Claims 12, 15, 20, 52, 56, 62, 69 and 70 have been amended. Thus, Claims 1-4, 12-16, 18-20, 38-42, 52-54, and 56-70 are pending in the present application. Support for the claim amendments may be found in the specification at, for example, page 9, paragraph [0041] and page 10, paragraph [0043] . Accordingly, no new matter has been added. Please note that all references to the specification set forth in this amendment are to the substitute specification filed January 17, 2005. Reconsideration and withdrawal of the present rejections in view of the following amendments and comments are respectfully requested.

Rejections under 35 U.S.C. 112, first paragraph

Claims 12, 15, 16, 18-20, 42, 52-54, 56, 60-67 and 69-70 were rejected under 35 U.S.C. 112, first paragraph, for allegedly lacking enablement. The Examiner contends that while the specification is enabling for methods using a peptide having the structure B1-$(X)_n$-Asn-Q in which Q is a vinylmethylsulfone, chloromethylketone or fluorometylketone, does not reasonably provide enablement for any AEP inhibitor comprising any other "group capable of reacting with an active site cysteine of asparaginyl endopeptidase", and that the specification does not adequately define what constitutes "Q" or "the group". In addition, the Examiner states that the metes and bounds of the phrase "reacting with" have not been established in the specification, and that the only reactive groups disclosed are vinylmethylsulfone, chloromethylketone and fluoromethylketone.

The claims as amended recite that the group in question is capable of reacting with the active site cysteine of asparaginyl endopeptidase and forming a covalent complex therewith. The recitation of forming a covalent complex should address the Examiner's concerns regarding the metes and bounds of the phrase "reacting with." The formation of a covalent complex is supported in the specification at page 9, paragraph [0041] and page 10, paragraph [0043].

Contrary to the Examiner's assertion, the specification discloses numerous reactive groups ("Q" or "the group") in addition to vinylmethylsulfone, chloromethylketone and fluoromethyl ketone. For example, the specification at page 9, paragraph [0039] lists the following irreversible AEP inhibitors which will react with the active cysteine residue at the active site of AEP and are therefore encompassed by the pending claims: peptide aldehydes,

peptide diazomethanes (diazomethyl ketones), peptide (acyloxy)methanes, peptide N, O diacyl hydroxamates, peptide nitriles, peptide I-keto carbonyls, peptide ketomethylsulfonium salts and peptide epoxides. Specific examples of these additional AEP inhibitors may be found in the t specification at pages 10-11, paragraphs [0047]-[0051] (peptide aldehyde inhibitors); page 12, compounds (i)-(iii) (peptidyl diazomethanes); pages 13-14, compounds (i)-(v) (peptidyl(acyloxy)methanes); pages 14-15, compounds (i)-(iv) (N,O-diacyl hydroxamates); pages 15-17, compounds (i)-(iv), E-64, leupeptin, antipain, elastinal. Some of these inhibitors are additionally described in the specification at pages 18-19. Thus, the definition of "Q" and "the group" is well defined by the specification.

One of ordinary skill in the art would have no difficulties in practicing the invention as presently claimed by using any of the protease inhibitors mentioned above. These compounds are all well known in the art, and exert their inhibitory activity by binding to an active site cysteine residue. Thus, their use in the present invention would not require undue experimentation as alleged in the Office Action. Although specific reaction conditions (e.g., amounts of inhibitor and reaction time) may need to be optimized for each specific inhibitor within the scope of the claims, such experimentation is routine and can easily be performed by one of ordinary skill in the art. Thus, the specification provides ample teaching how to make and use the invention as presently claimed.

In view of the comments presented above, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

Rejections under 35 U.S.C. 112, second paragraph

Claims 13 and 14 were rejected under 35 USC 112, second paragraph, as being indefinite based on recitation of "an effective amount of an agent for the prevention...of an autoimmune disease or an allergic or hypersensitivity reaction" (Claim 13) and "an effective amount of an immunosuppressive agent" (Claim 14). The Examiner states that if the purpose of administering AGNK or KNNE is for inhibiting the immune response, then it is unclear why the additional agents would be administered.

The specification at page 27, paragraph [0101], describes the use of AEP inhibitors for treating allergies and allergic reactions and hypersensitivity reactions. The specification at page 28, paragraph [0105], discusses the use of AEP inhibitors for immunosuppression. Since the

specification describes the use of AEP inhibitors in these capacities, the administration of AEP inhibitors in combination with an agent for the prevention, treatment or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction (claim 13) or with an immunosuppressive agent (claim 14) is fully definite since the purpose of administering the AEP inhibitor is the same as the purpose of administering the additional compounds recited in these claims. In fact, the specification explicity discloses the co-administration of AEP inhibitors and these additional compounds (page 28, paragraphs [0103] and [0106]).

In view of the comments presented above, Applicant respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. 112, second paragraph.

CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited.

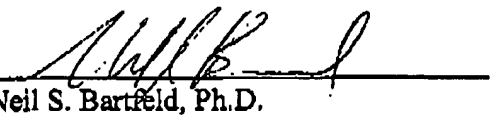
The undersigned has made a good faith effort to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully invited to call the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 19, 2006

By: 

Neil S. Bartfeld, Ph.D.
Registration No. 39,901
Agent of Record
Customer No. 20,995
(619) 235-8550

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